

Appl. No. : 10/063,602  
Filed : May 3, 2002

### REMARKS

In response to the final Office Action dated March 6, 2006, Applicants submitted an RCE and an amendment and response on July 5, 2006. No further Action has been issued. Further to the final Office Action mailed March 6, 2006, and in supplement of the submission of July 5, 2006, Applicants submit the following remarks, which Applicants respectfully request be approved for entry into the record.

#### Rejection Under 35 U.S.C. §101 – Utility

The PTO has rejected Claims 1-5 under 35 U.S.C. § 101 as lacking a specific and substantial asserted utility or a well established utility.

##### PTO Arguments in rejecting the claims

Applicants understand the PTO to base the rejection on two main arguments:

1. The PTO challenges the reliability of the evidence reported in Example 18, stating that the countervailing evidence shows that the skilled artisan would not know if the disclosed change in PRO1328 transcripts is tumor-dependent or tumor-independent;
2. The PTO argues that protein expression levels are not predictable from the mRNA expression levels.

#### The PTO has Concluded that the data in Example 18 are Sufficient to Establish the Utility of the Claimed Invention

As an initial matter, Applicants point out that in other applications filed by Applicants that rely on data from the exact same disclosure, Example 18, and in which Applicants have submitted substantially the same references in support of their asserted utility, the PTO has concluded that: “[b]ased on the totality of evidence of record, one of skill in the art would find it more likely than not that an increase in message as measured by RTPCR would be predictive of an increase in protein expression levels, absent evidence to the contrary. Therefore, the data presented in Example 18, which demonstrates differential expression of nucleic acids encoding PRO1180, also supports a conclusion of differential expression of PRO1180 polypeptide. Therefore, one of ordinary skill in the art would be able to use the PRO1180 polypeptide diagnostically for distinguishing normal kidney and rectal tumor tissues compared to kidney tumor and normal rectal tissue, as asserted by Applicant.” See *Examiners*

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*Reasons for Allowance* in pending Application No. 10/063,529. See also *Examiners Reasons for Allowance* in Application No. 10/063,530, No. 10/063,524, No. 10/063,582, and No. 10/063,583, all of which conclude that the data presented in Example 18, which demonstrate differential expression of the nucleic acids encoding certain PRO polypeptides, also support a conclusion of differential expression of the PRO polypeptides, making the claimed PRO polypeptides and antibodies that bind the PRO polypeptides useful for diagnostic purposes.

Applicants therefore request that the Examiner recognize the utility of the claimed invention, supported by the data presented in Example 18 and Applicants numerous cited references, as was done in the other applications referenced above.

*Applicants' arguments and rebuttal evidence*

Applicants' previous response submitted on July 5, 2006 fully addresses the PTO's first argument regarding the disclosed change in PRO1328 transcripts. No further information or remarks are submitted herewith regarding the PTO's first argument.

In addressing the PTO's second argument regarding the relation between differential mRNA levels and protein levels, Applicants have previously addressed the issues presented in the references cited by the PTO. Applicants also previously submitted declarations and scientific publications that support Applicants' position. The details of the teachings of these declarations and references, and how they support Applicants' asserted utility, are of record and will not be repeated here. In further support of Applicants' assertions that differential mRNA levels generally lead to corresponding differential protein levels, Applicants submit the following Declaration and remarks as a supplement to those submitted in the response filed July 5, 2006.

Applicants enclose herewith a copy of a declaration by Randy Scott, Ph.D. (attached as Exhibit 1). Dr. Scott is an independent expert in the field of molecular diagnostics, with over 15 years experience. He is the author of over 40 scientific publications in the fields of protein biology, gene discovery, and cancer, and is an inventor on several issued patents. His curriculum vitae is attached to the declaration. In paragraph 10 of his declaration, Dr. Scott states:

One reason for the success and wide-spread use of the DNA microarray technique, which has led to the emergence of a new industry, is that generally there is a good correlation between mRNA levels determined by microarray analysis and expression levels of the translated protein. Although there are some exceptions on an individual gene basis, it has been a consensus in the scientific community that elevated mRNA levels are good predictors of increased abundance of the

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corresponding translated proteins in a particular tissue. Therefore, diagnostic markers and drug candidates can be readily and efficiently screened and identified using this technique, without the need to directly measure individual protein expression levels. *Scott Declaration* at ¶10 (emphasis added).

Applicants submit the opinion of yet another expert in the field that changes in mRNA level for a particular protein in a given tissue generally lead to a corresponding change in the level of the encoded protein. Importantly, Dr. Scott also states that, contrary to the contentions of the PTO, diagnostic markers can be identified "without the need to directly measure individual protein expression levels." This opinion is supported by Dr. Scott's extensive experience in the field, as well as the fact that an entire industry has developed around technology to assess differential mRNA expression. As stated previously, there would be little reason to study changes in mRNA expression levels if those changes did not result in corresponding changes in the encoded protein levels.

Applicants submit that the evidence and arguments of record, as supplemented with the Scott declaration and arguments submitted herein establish that it is more likely than not that one of skill in the art would believe that because the PRO1328 mRNA is differentially expressed in lung tumor and melanoma tumor tissue compared to normal lung and skin tissue, the PRO1328 polypeptide will likewise be differentially expressed in lung and melanoma tumors. This differential expression of the PRO1328 polypeptide makes the claimed antibodies that bind to the PRO1328 polypeptide useful as diagnostic tools for cancer, particularly lung and melanoma cancer.

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**BEST AVAILABLE COPY****CONCLUSION**

In view of the above, Applicants respectfully maintain that claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues may be resolved by telephone.

Please charge any necessary fees, including any fees for additional extension of time, or credit overpayment, to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Sept. 11, 2006

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